REMARKS

The Office Action of December 29, 2009, has been carefully studied. Claims 10, 12-14, and 17-19 currently appear in this application. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration and formal allowance of the claims.

Interview Summary

Applicant's attorney wishes to thank Examiner Qazi for the courtesies extended during the personal interview of March 23, 2010. During that interview it was agreed that subsisting "formation" for "generation" would obviate the rejections under 35 U.S.C. 112, first and second paragraphs, and that "under shading" really means "in the absence of light." Examiner Qazi requested a showing that "improvement" was in the specification as filed.

There was no agreement with respect to the art rejections.

Rejections under 35 U.S.C. 112

Claims 12, 13 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

This rejection is respectfully traversed.

Suppressing the generation is described at page 2, last paragraph, states:

> Therefore, to produce ED-71 preparations, it is also important in practice to not only enhance the storage stability of ED-71 serving as an active ingredient, but also to suppress the generation of main degradation products.

That is, the invention relates to suppressing the formation or degradation products, in particular, the formation of trans ED-71 and the tachy form of ED-71.

The term "generation" has been replaced by "formation."

The specification mentions "under shading" a number of times, and specifically in Tables 2 and 3 on page 27. In these tables, vials of soft capsules containing Ed-71 were stored under 30°C 60% RH and [under] shading. That is, the vials were stored away from light, i.e., shaded. There is no specific requirement for temperature.

The Examiner alleges that there is no method for "improvement" in the disclosure. It is respectfully submitted that claim 18 is in standard Jepson form, that is, In United States patent law, a Jepson claim is a method or product claim where one or more limitations are specifically identified as a point of novelty, distinguishable over at least the contents of the preamble. They may read, for instance, "A system for storing information having (...) *wherein the*

improvement comprises:." The claim is named after the case, *Ex parte Jepson*, decided in 1917.

In a crowded art, a Jepson claim can be useful in calling the examiner's attention to a point of novelty of an invention without requiring the applicant to present arguments and possibly amendments to communicate the point of novelty to the Examiner.

The specification at paragraph 0019 discusses the advantages of the invention, one of these advantages being the use of the trans form of ED-71 as a material for the synthesis of various types of vitamin D compounds. Since this is an advantage of the invention, it is clearly an improvement in methods of synthesizing vitamin D compounds.

Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is respectfully traversed.

The term "generation" in claim 12 means the formation or production. That is, the presently claimed invention, as described at paragraph 0014. The generation of degradation products, namely, tachysterol and trans ED-71 , is suppressed. That is, the formation of this degradation product during

storage of the active ingredient, is suppressed. The term "generation" has been replaced by "formation."

"Shading," that is, "under shading" in claim 13, means that the composition is stored in the absence of light, i.e., under shade.

The "improvement" in claim 18 is that, in a standard method for synthesizing vitamin D compounds, the intermediate compound used in the synthesis is (5E,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol.

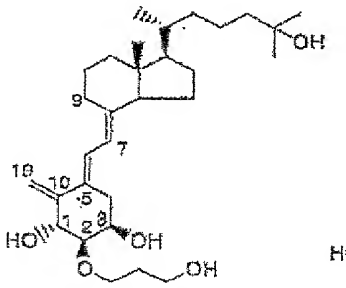
Art Rejections

Claims 10, 14, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamauchi, US 6,448,421.

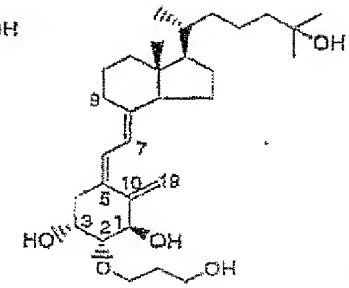
This rejection is respectfully traversed.

(5Z,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol, ED-71, can decompose to 6E-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10 (19)-triene-1,3,25-triol, the tachysterol of ED-71 and/or to o(5E,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10 (19)-triene-1,3,25-triol, the trans form of ED-71.

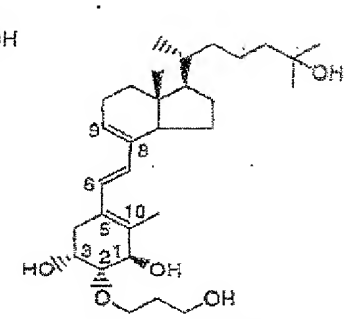
These compounds and their chemical structure are shown in the present specification, for example, at paragraphs 0007-0011 and 0028-0032. Their chemical formulas are provided below:



1: Trans form of ED-71
(5E form)



2: ED-71
(5Z form)



3: Tachysterol form of ED-71

As can readily be seen from the chemical formulae, these compounds differ in the configuration at the 5-position or in the location of existing double bonds. Furthermore, these compounds actually exist as separate compounds. For example, each of the compounds can be separated from the other by, for example, chromatography, as shown in Figures 1 and 2 of the present specification.

Yamaguchi discloses preparation and purification of ED-71. In contrast thereto, the present claims are directed only to the trans form of ED-71, that is, the 5Z-form. Claim 10 is drawn to a composition containing the trans form of ED-71, and claims 12 and 13 are drawn to a method for suppressing the formation of the trans form. In claim 14, the trans form is used as a standard for the degradation product. Claim 17 and 18 are directed to methods of synthesizing vitamin D compounds using the trans form as an intermediate.

As has been discussed at length in the prosecution of these claims, the trans form of ED-71 is a completely different compound from ED-71 itself.

It is believed that the Examiner understands that either of (5Z,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10 (19)-triene-1,3,25-triol or of (5E,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10 (19)-triene-1,3,25-triol recited in the claims is the tachy form of ED-71. This is because the Examiner refers to tachysterol of formula III disclosed in Yamaguchi, which she alleges anticipates the claimed invention. However, neither of these two compounds is the tachy form of ED-71. Correctly, (5Z,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10 (19)-triene-1,3,25-triol is ED-71 and (5E,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10 (19)-triene-1,3,25-triol is the trans form of ED-71.

Thus, Yanauchi does not anticipate the herein claimed invention, as Yamauchi does not disclose a method for suppressing the formation of a degradation product of ED-71.

In *Sanofi-Synthelabo, Sanofi-Synthelabo Inc, v. Apotex, Inc.*, 550 F.3d 1075; 89 USPQ2d 1370 (Federal Circuit 2008), the court held that the district court was correct in its holding that the dextrorotatory isomer was patentable in view of its known racemate described in earlier patents. As in the present case, the new isomer has different properties from the known compound. Therefore, it is respectfully submitted that the trans form of ED-71 is patentable over ED-71, and withdrawal of the rejection is earnestly solicited.

Claims 10, 14, 17 and 18 are rejected under 35 U.S.C. 102(b) as anticipated by Miyamoto, *Chem. Pharm. Bull.* and Miyamoto et al., US 4,666,634.

The Examiner alleges that because the references disclose a method for producing ED-71 they inherently disclose the presently claimed invention.

This rejection is respectfully traversed.

Miyamoto discloses vitamin D analogues that have a hydroxy group at the 2-position. The presently claimed invention relates to stabilizing preparation containing ED-71 as well as standards for assaying for degradation products of ED-71. The trans form of ED-71, which is the most significant degradation product, can be used both in the analysis of an ED-71 preparation to gauge its stability, and as a material for synthesizing various types of vitamin D-based compounds (page 6, paragraph 0019).

The trans form of ED-71 and the tachysterol form of ED-71 are not the same compounds disclosed by Miyamoto, and it is not understood how the Examiner can allege that Miyamoto anticipates the herein claimed invention. As noted above, a compound can be patentable over a known isomer of the compound.

Claims 10, 12-14, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamauchi, Miyamoto, and Miyamoto (*Chem. Pharm. Bull.*) and Chen et al., WO 03/047595.

This rejection is respectfully traversed.

As noted above, neither Yamauchi nor Miyamoto discloses the trans form of ED-71.

The Examiner has cited column 19, lines 35-41, as teaching the products. It appeasers that column 19, lines 45-50, is the passage that is relevant, which passage states that the tachy and lumi forms and the pro-form of ED-71 are useful for a test or analysis which may be carried out in the synthesis of a vitamin D derivative. However, this says nothing at all about measuring degradation or ED-71 during storage, nor of the trans form itself.

Chen states at paragraph 0056, "The pharmaceutical compositions of the present invention may further comprise one or more additives. Additives that are well known in the art include, e.g., antioxidants, ..." However, it was general technical knowledge at the time of completion of the present invention that antioxidants added to suppress generation of oxides, that is, to prevent oxidation of compounds in a system. Thus, one skilled in the art reading Chen would assume that the antioxidants were added to prevent oxidation of vitamin D compounds.

Miyamoto only discloses compounds of the 5Z form, and Miyamoto fails to disclose any compounds of the 5E form, as claimed herein.

In contrast thereto, the decomposition products to be suppressed in the presently claimed compositions are not oxidation products, the formation of which would be suppressed by antioxidants, but are the trans form of ED-71 and

the tachysterol form of ED-71. These decomposition products are not oxides of ED-71, but are isoforms of ED-71. These decomposition products have neither an increased number of oxygen atoms nor a reduced number of hydrogen atoms, which would be the result of oxidation of ED-71. However, it has been demonstrated that dl-α-tocopherol is far superior to other antioxidants in suppressing summarization of ED-71.

In the supplemental remarks filed March 26, 2008, the declaration of Hitoshi SATO, one of the inventors of the present application, was submitted. In this declaration, Mr. SATO provided evidence showing that the trans form of ED-71 exhibited a relative differentiation-inducing activity of HL-60 cells that was nearly 20 times greater than the parent compounds, ED-71. It is clear from this declaration that the trans form of ED-71 is not obvious over the parent compounds.

In responding to the remarks made in the amendment filed October 14, 2009, the Examiner alleged that both 5E,7E and 5Z,7E are known, citing WO2005/074943. However, this publication is based on the same priority document as the present application, and one would expect it have all of the same information as in the present specification. Because this publication is based upon the same priority document as the present application, it is respectfully submitted that this publication cannot sever as evidence that the trans form of Ed-71 was known.

With respect to the difference between ED-71 and the trans form of ED-71, it is not required that the specification provide evidence of the differences. That is exactly why the declaration of Hisakazu Katsuki was submitted with the amendment filed August 20, 2009. That declaration demonstrated that that these two compounds have greatly different properties in differentiation. This is all that is required by the *Sanofi* decision cited above to differentiate the trans form of ED-71 from Ed-71.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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